HEMODYNAMIC CHANGES IN THE SMALL VESSELS IN MAN AS ANALYZED BY DIGITAL PLETHYSMOGRAPHY

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Although fairly adequate methods are available for the study of the hemodynamics of the arterial circulation and overall blood flow to various areas, little is known of the dynamic changes which occur in the small vessels in man. Aside from the observations of Thomas Lewis (1) on the terminal circulation in the human skin, and measurements of static capillary pressure by Landis (2), further explorations have been hampered by the lack of suitable methods of study. On the other hand much has been learned about the minute vessels from investigations in living animals and from anatomic specimens.

Anatomically the capillary bed begins with the metarterioles which arise as branches or prolongations of the terminal arterioles. The metarterioles form the initial portions of the so-called preferential or thoroughfare channels described by Chambers and Zweifach (3) which, after a relatively long course, join similar channels and terminate in the venules. Numerous sphincteric muscular buds, the precapillary sphincters (4), which originate at various intervals along the early portion of the thoroughfare channels, make up the proximal ends of the true capillaries. These small endothelial vessels in turn empty into the distal segments of the same or other thoroughfare channels. In addition to these components of the small vessel unit there occasionally are relatively large short vessels, the arteriovenous anastomoses, which arise from metarterioles or arterioles and empty directly into venules.

Changes in the diameter of the proximal portions of the thoroughfare channels permit flow through these vessels to be independent of pressure and flow conditions in the systemic circulation. Further, the pulsatile quality of the blood flow in the larger arterial vessels is replaced by a relatively continuous flow through the thoroughfare channels. Alternate opening and closing of the precapillary sphincters produces an intermittent type of flow through the capillaries. These alternating periods of spontaneous constriction and relaxation of the metarterioles and of the precapillary sphincters, a process known as vasomotion (5), allows adjustment of the circulation through the capillary unit as necessary to provide for the metabolic requirements of the tissue at any moment and in the skin to serve as radiators of body heat. The arteriovenous anastomoses (6) are usually closed during normal conditions but open under special circumstances of blood flow.

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During the course of studies on the effects of drugs on the digital plethysmo-gram certain consistent patterns of blood flow, pulse volume and digital volume were observed depending upon the agent being used. The analysis of these patterns suggested a relationship to hemodynamic changes in the small cutaneous vessels. The purpose of this report is to present an interpretation of these ple-thysmographic patterns in terms of changes in the small vessels and to correlate this data with direct observations of the vasculature of the bulbar conjunctiva.

METHODS

Blood flow, digital volume, and pulse volume were measured in the large toe of young normal subjects using a Burch-Winsor portable plethysmograph (7). Digital blood flow was measured by the venous occlusion method (8) using a congesting cuff placed at the base of the digit or at the ankle and inflated to 15 to 20 mm. Hg below the diastolic blood pressure. When technically possible, occlusion at the base of the digit was carried out. However, with high rates of blood flow occlusion at the base of the digit produced such a rapid increase in digital volume that accurate measurements of flow were not possible. Under these conditions it was necessary to use the occluding cuff at the ankle and the values so obtained were multiplied by 3 as suggested by Goetz (9). Although the ratio between digital and ankle occlusion appeared to vary somewhat in different individuals and with varying rates of blood flow in the same individuals, a factor of 3 appeared to be sufficiently accurate for purposes of comparison.

Large changes in digital volume could not be accommodated in the plethysmo-graph without adjusting the position of the volume-recording aluminum capsule upon which the bowstring assembly was mounted. Since this adjustment pro-duced a change in the sensitivity of the recorder a slight modification of the machine was necessary in order to measure volume changes without altering any of the adjustment mechanisms. Accordingly a horizontally placed pipette with 0.01 cc graduations and containing a drop of mercury was incorporated into the pneumatic system. By manipulation of the plunger of a tuberculin syringe attached permanently to the distal end of the pipette the mercury column could be moved a measurable distance to accommodate for changes in the volume of the digit, thus affording a quantitative determination of digital volume at any time.

The direct recording of arterial pressure (10) and the estimation of foot blood flow and skin temperature were determined according to methods de-scribed elsewhere (11). Determinations were made in a constant environmental temperature of 68 to 70°F. Control values were obtained only after the subject had been at rest in the supine position for at least 45 minutes. The foot of the bed was elevated on 2-inch blocks to minimize the effects of postural hypoten-sion. Blood flow was determined at frequent intervals and each value represented the average of two or more closely spaced observations.

Direct observation of the bulbar conjunctiva was made using a Bausch and Lomb binocular dissecting microscope with a magnification of 30 X. However, it was not possible to obtain sufficient illumination to take photographs through

the microscope. Hence, these were taken directly using a Leica 35 mm. camera with a 180 mm. extension tube and a 9 cm. Elmar Leitz lens. Illumination was furnished by a Bardwell-McAllister Baby Keg-Lite with a 750 watt lamp equipped with a Foco-spot. Exposures were made on Panatomic film with a lens opening of f. 4 at 1/100 second. The final magnification after further enlargement of the films was 15 X.

RESULTS

Digital Blood Flow, Digital Pulse Volume, and Femoral Pulse Pressure after C6 as Compared to Lumbar Epidural Block

In normal subjects who were given 50 to 100 mg of C6 intravenously and on another day lumbar epidural block, the increases in toe blood flow were essen-

TABLE I

Effects of hexamethonium, lumbar epidural block and priscoline on digital volume, digital pulse volume, and digital blood flow

PROCEDURE	NUMBER OF CASES	DIGITAL VOLUME		DIGITAL PULSE VOLUME*		DIGITAL BLOOD FLOW*	
		Average Maximum Increase cc per 10 cc	Average Time Reach Maximum Minutes	Average Maximum cc per 10 cc	Average Time to Reach Maximum Minutes	Average Maximum cc per 10 cc per Minute	Average Time to Reach Maximum Minutes
Hexamethonium (C6) (Intravenously)........	10	1.1	15	0.25	15	4.7	35
Lumbar Epidural Block..	7	1.1	25	0.36	20	4.9	40
Priscoline (Intraarterially)..................	3	0.8	7	0.12	5	1.1	15

* Average values during control period were for pulse volume 0.001 cc. per 10 cc. of digit and for blood flow 0.14 cc. per 10 cc. of digit per minute.

tially similar either after C6 or after lumbar block, the maximum flows in each instance averaging 5 cc per 10 cc of digit per minute (Table I, Fig. 1). The blood flow of the entire foot as determined in the opposite extremity also indicated no significant difference between the increase in flow after C6 and after lumbar block (11). However, digital pulse volume always was 30 to 50 per cent greater after lumbar block than following C6 (Table I, Fig. 1).

Since it appeared possible that the relatively smaller pulse volume after C6 compared to lumbar block might be due to the effect of this agent on arterial pulse pressure, the plethysmographic studies were repeated with simultaneous measurement of femoral arterial pressure in the limb under study using a hypodermic manometer. After C6 there was a significant fall of arterial pressure, especially of the systolic pressure, and an increase in heart rate producing a rather marked decrease in pulse pressure (Fig. 2). Slight decreases of both systolic and diastolic pressures without change in heart rate were observed in the femoral artery after lumbar block but this did not produce any significant changes in pulse pressure.
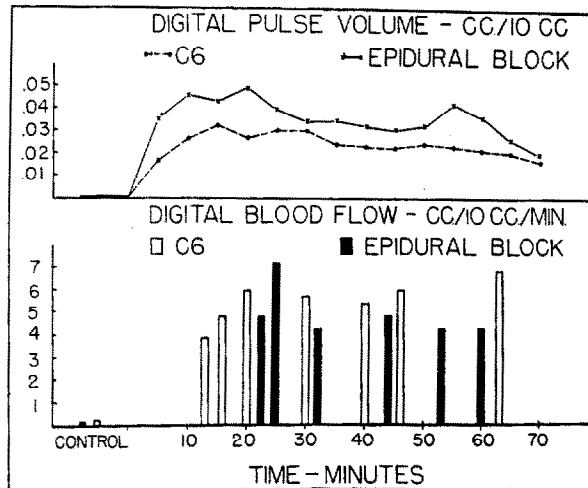
Fig. 1. Chart comparing the effects of the intravenous injection 50 mg of C6 ion and the lumbar epidural injection of 600 mg of Metycaine on digital pulse volume and blood flow in subject R. B., a normal male, age 29 years.
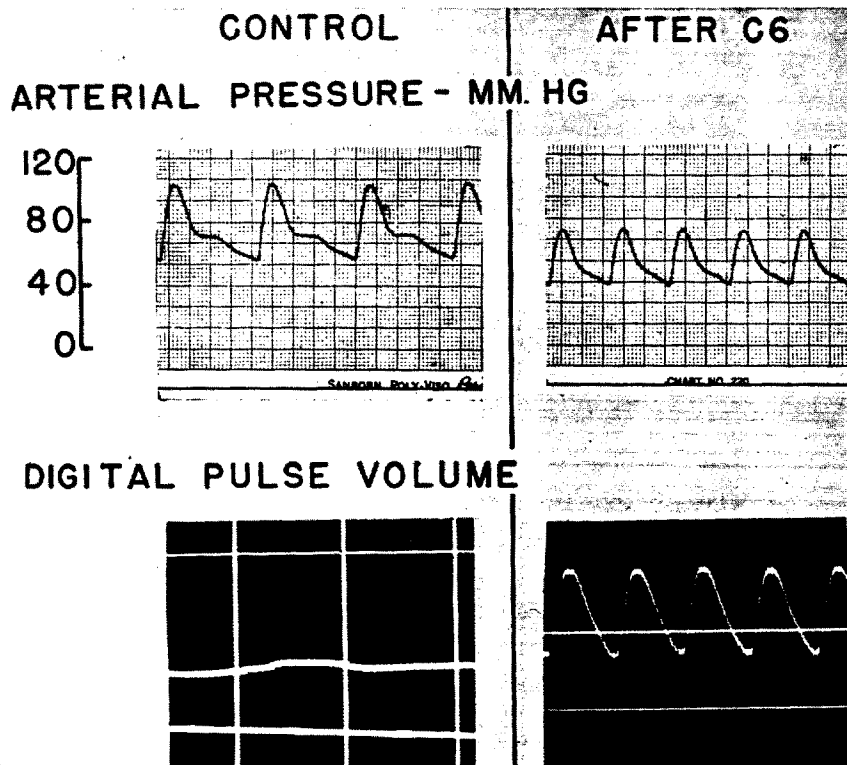

Fig. 2. Cuttings from the tracings of femoral arterial pressure and digital pulse volume before and after the intravenous injection of C6 ion in subject P.S., a normal male, age 25 years. The plethysmographic tracing in the control is at a slow paper speed and after C6 at a rapid speed. During the period of maximum increase in pulse volume there is considerable decrease in arterial pressure, especially pulse pressure.

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*Differential Changes in Digital Volume, Pulse Volume and Blood Flow after C6
or Lumbar Block in Relation to Time. Vessels of the Bulbar Conjunctiva*

Following C6 there was a rapid increase in both digital and pulse volumes beginning within 5 minutes after intravenous administration of the drug and reaching maximum values by the end of 15 or 20 minutes. However, the rate of increase of digital blood flow was considerably slower as compared to pulse and digital volumes, and maximum values for blood flow usually occurred by the end of 30 to 40 minutes or even longer (Fig. 3). Pulse volume always had leveled off and frequently was decreasing before the greatest elevation of blood
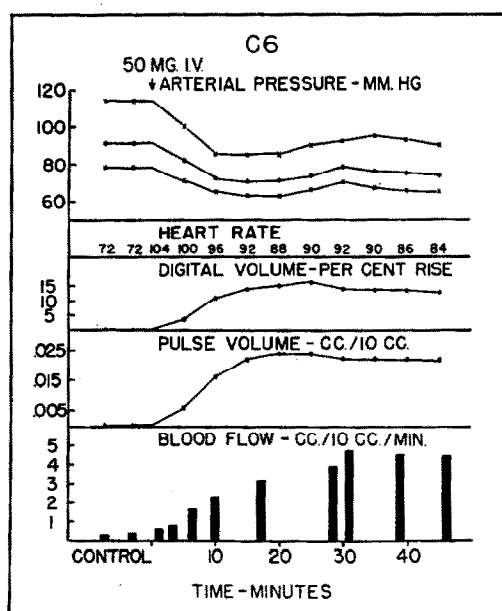

FIG. 3. Chart of the femoral arterial pressure, heart rate, digital volume, pulse volume and blood flow before and after the intravenous injection of 50 mg. of C6 ion in subject P. S. The middle line in the chart of arterial pressure represents the mean arterial pressure. The maximum increases in digital and pulse volumes precede the maximum increase in blood flow.

flow had occurred. A similar sequence was observed after lumbar block although the time of onset and of maximum values occurred slightly later. Thus, blockade of sympathetic vasoconstrictor impulses to the digit, whether by C6 or lumbar block, always produced a rapid and early increase in pulse volume and more gradual increase in blood flow.

Direct observations of the conjunctival vessels were made before and after C6 using a dissecting microscope. While magnification was not sufficiently high to observe details of capillaries or to identify arteriovenous anastomoses, changes in the venules and arterioles were readily discerned (Fig. 4). Within 10 minutes after the intravenous administration of C6 there was a marked increase in the size of and pulsations in the larger arterial vessels. Smaller arteriolar branches also became readily visible. At the end of 20 minutes there was an increase in

the number of the smallest vessels visible and concurrently pulsations in the larger arterial vessels became fainter. After 30 minutes the larger arterial vessels had decreased in size and pulsations were less readily visible. At the same time there was a marked increase in the number of small vessels with formation of a dense network. At this time the veins greatly exceeded in size the larger

CONTROL   **6 MIN. AFTER C6**

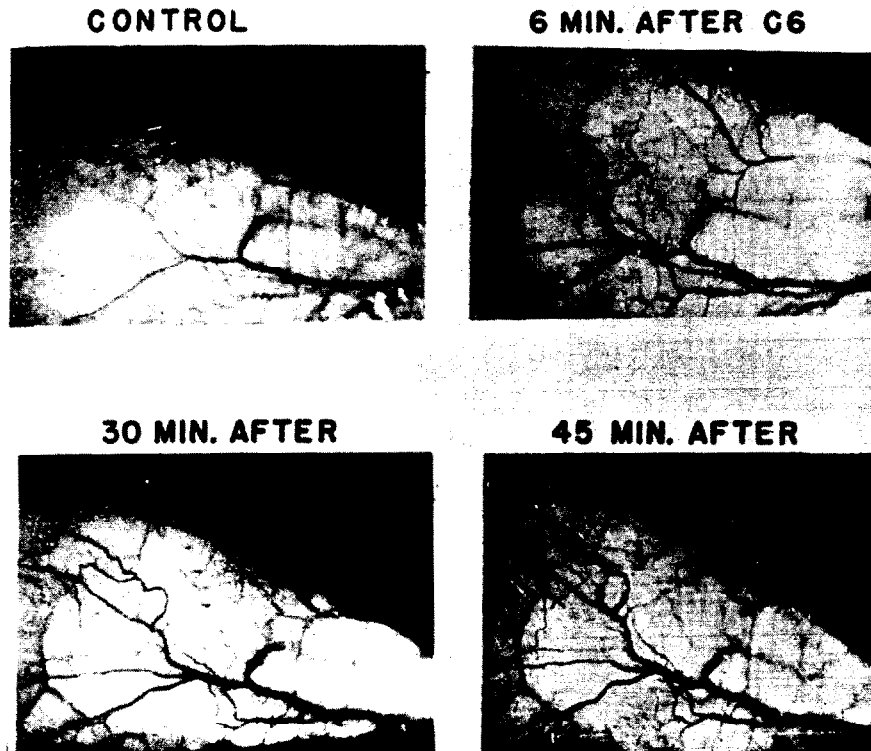**30 MIN. AFTER**   **45 MIN. AFTER**

FIG. 4. Photographs of the bulbar conjunctiva taken before and at intervals of 6, 30 and 45 minutes after the intravenous injection of 50 mg. of C6 ion in subject J. McG., age 30 years. A large vein drains the area from left to right and is accompanied by an artery which is only faintly visible during the control period. Six minutes after C6 the artery and its branches have become much larger, while in the later photographs the network of smaller vessels has increased greatly in extent and the artery again has become faintly visible. See text for further details.

arterial vessels which accompanied them. Later at the end of 45 minutes the network of small vessels was even denser than previously. The veins became somewhat larger but even more striking was the decrease in the size of the arterial vessels to a point where they were barely visible (Fig. 3).

Effect of Intraarterial Priscoline on the Digital Plethysmogram and Conjunctival Blood Vessels

When 50 mg of Priscoline were injected over a period of 4 minutes into the femoral artery of the extremity under study there was only a slight increase

in pulse volume to an average maximum of 0.12 cc per 10 cc of tissue after 5 minutes. The rate of blood flow likewise showed very little increase and reached after 15 minutes an average maximum of only 1.1 cc per 10 cc per minute. By contrast to these minor changes in pulse volume and blood flow there occurred within 7 minutes a rapid and marked increase in digital volume comparable to that which occurred after C6 (Table I, Fig. 5). The striking increase in digital volume was continguous with the period of intense flushing of the skin observed after intraarterial Priscoline. This degree of flushing was not observed after C6 or epidural block.
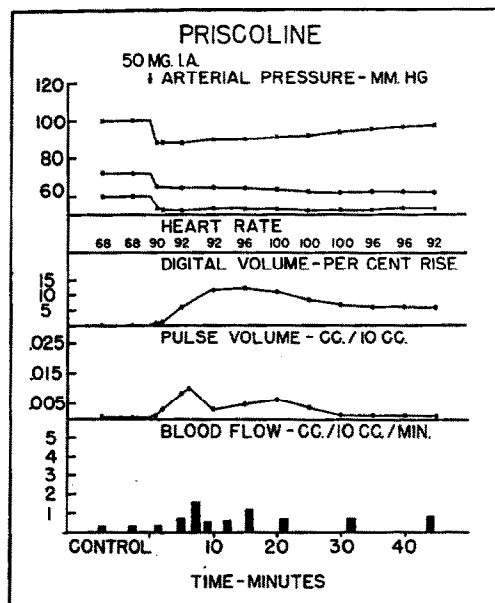

Fig. 5. Chart of the femoral arterial pressure, heart rate, digital volume, pulse volume and blood flow before and after the intraarterial injection of 50 mg. of Priscoline in subject R. B. Comparison with changes after C6 in this subject (See Fig. 1) indicate far less increase in pulse volume and blood flow after Priscoline, yet digital volume rose to values approximating those observed after C6.

Direct observation of the bulbar conjunctival vessels with a dissecting microscope was made after intravenous injection of 50 mg of Priscoline. At the end of 10 minutes, and during the time that facial flushing was present, there was an increase in the size of the large venous channels. Small straight branches extending from the largest vessels became visible. After 15 minutes there was a further slight accentuation of these changes and some increase in the number of small vessels with formation of a vascular network. The degree of increase in vascularity was far less than that seen after C6. At the end of 25 minutes there was very little change as compared to 15 minutes and by 35 minutes there was a definite decrease in the number of the smallest vessels. Although the larger venous channels still appeared distended, all other visible vessels had diminished in size.

DISCUSSION

Digital pulse volume frequently has been employed as an index of blood flow in the digit (12, 13). Under certain conditions a constant relationship between these two factors may exist, but under the conditions of the present studies increases in pulse volume could not be interpreted as denoting a proportionate increase in blood flow. When C6 and lumbar epidural block were compared for their effects on the digital plethysmogram it was found that maximum pulse volume in the toe always was $\frac{1}{3}$ to $\frac{1}{2}$ greater after epidural block than after C6 although blood flow was increased to essentially the same degree after either procedure. Had the pulse volume alone been used to estimate blood flow it would have been erroneously concluded that blood flow was consistently much greater after lumbar epidural block than after C6. Other studies in this laboratory (14) have disclosed a similar discrepancy between pulse volume and blood flow in the finger after C6 as compared to stellate block.

Since blood flow was the same both after C6 and after epidural block with Metycaine, it was obvious that pulse volume is related to factors other than blood flow alone. Thus, (1) pulse volume is, in actuality, a reflection of changes in the larger arterial vessels since pulsatile flow does not occur beyond the terminal arterioles, and (2), it undoubtedly is related to pulse pressure since the greater the spread between systolic and diastolic pressure, the more bounding will be the pulse. Since hexamethonium, unlike epidural block produced a marked reduction in pulse pressure it was reasonable to believe that this was the major factor in the production of the smaller pulse volume following C6 as compared to epidural block.

It was noted that the early increase in digital pulse volume after sympathetic blockade produced either with C6 or epidural injection of Metycaine could not be explained by changes in arterial pulse pressure alone because the period of greatest pulse volume occurred at the time when the pulse pressure was the smallest. Likewise the early elevation of pulse volume occurring after C6 or epidural block could not have resulted from a sudden release of peripheral resistance since blood flow did not reach maximum values until 15 or more minutes later. Some other local change must have occurred to make the flow more pulsatile.

The early and marked increase in digital pulse volume seemed best explained by assuming that the initial change following sympathetic blockade is a dilatation of the larger vessels on the arterial side and of the arteriovenous anastomoses rather than of the capillaries. By restricting blood flow primarily to the larger vessels the force of the pulse pressure would not be damped out by passage through the more minute vessels. Further support of the concept of primary dilatation of the larger vessels and more direct communication between arteries and veins is furnished by previous observations that following another "sympatholytic" agent, dihydroergocornine (DHO), perceptible pulsations appeared in the venous pressure recordings taken from an antecubital vein at the time of increase in pulse volume in the finger (15).

It is also necessary to explain the later occurrence of a further increase in blood flow without change or a slight decrease in pulse volume following sympa-

thetic blockade. In order to explain the relatively late increase in blood flow one must postulate a further decrease in peripheral resistance. Such could be accomplished if at this later stage there occurred a relaxation of the precapillary sphincters. Such an event would not only result in a greatly augmented blood flow but also would dampen out the increased pulse volume since passage through these small channels would convert the pulsatile flow into a more continuous stream.

From the analysis of sequential plethysmographic changes, therefore, it was inferred that the earliest major change collowing sympathetic blockade either with C6 or lumbar epidural anesthesia was dilatation of the arteries, arterioles and A–V anastomoses. At a later stage there occurred dilatation of a maximal number of precapillary sphincters. During the entire process of small vessel relaxation there must have been an accelerated decline in local peripheral resistance which reached its lowest value at the time of greatest dilatation of the precapillary sphincters. Both after epidural block and C6 a similar pulse volume-blood flow pattern was observed in relation to time with the greatest increase in pulse volume initially and later the maximum increase in digital blood flow.

Direct observation of the conjunctival vessels supported the inferences based on plethysmographic data. It was quite apparent that the larger arterial vessels dilated first, and only later did the "capillary lake" open up resulting in a rapid draining away of blood from the arterial supply. The early increase in size of the arterial vessels and the observation of increased pulsations therein coincided with the time of maximum increase in pulse and digital volumes observed in the plethysmogram, whereas the later appearance of a dense network of small vessels coincided with the time of maximum digital blood flow.

The small increase in digital blood flow which occurred after Priscoline indicated only a slight decrease in peripheral resistance. Similarly, the slight increase in pulse volume suggested that there was a minor degree of dilatation of the larger arterial vessels capable of carrying a pulsatile type of flow. However, a loss of venous tone and distention of the venous plexuses would account for the marked increase in digital volume. According to Sir Thomas Lewis the skin color is determined primarily by the amount of blood in the subpapillary venous plexuses. The period of intense flushing of the skin after Priscoline coincided in time with the period of rapid increase in digital volume and appeared to furnish further evidence for the validity of the plethysmographic analyses.

When the changes in the vessels of the bulbar conjunctiva were observed after Priscoline, it was seen that there was only slight dilatation of the vessels on the arterial side without visible pulsations. In addition the appearance of a dense network of small vessels such as was observed after C6 did not occur after Priscoline. The most marked change observed after Priscoline was dilatation and engorgement of the larger venous channels. From these observations of plethysmographic changes and visualization of the conjunctival vessels it is suggested that the primary action of Priscoline in the skin is on the venous side of the circulation and hence probably is not a result of the adrenergic blocking effects of the drug but rather of its histaminic action.

The concepts developed in this paper are not advanced as established facts but rather as hypotheses to serve as footholds for further investigation. Certain phenomena which we have observed to occur in consistent patterns have been subjected to analysis in the light of our present knowledge of the terminal circulation. It is hoped that analysis of the differential changes occurring in the digital plethysmogram followed by correlation with data obtained using other techniques such as direct microscopic observations may provide a method of studying the hemodynamics of the small cutaneous vessels in man.

SUMMARY AND CONCLUSIONS

Sequential changes occurring in the digital plethysmogram after administration of hexamethonium (C6), lumbar epidural block and Priscoline given intra-arterially were analyzed in terms of the hemodynamics of the small vessels of the skin. The vasculature of the bulbar conjunctiva was observed directly to confirm the changes of small vessels inferred from plethysmographic data.

1. Comparison of digital pulse volume and blood flow after sympathetic blockade indicated that pulse volume is not a reliable quantitative index of blood flow under these conditions. Pulse volume appeared to vary primarily with pulse pressure and dilatation of the larger vessels on the arterial side.

2. The plethysmographic changes after sympathetic paralysis either with C6 or epidural block followed a constant pattern with an early increase in digital volume and pulse volume to maximum values and later a maximum increase in digital blood flow. This plethysmographic pattern was interpreted as indicating an early dilatation of arteries, arterioles and A–V anastomoses followed later by relaxation of the precapillary sphincters. Direct observation of conjunctival vessels supported the concept of early relaxation and appearance of pulsations in larger arterial vessels and a later dilatation of the smaller vessels.

3. While pulse volume and blood flow were increased only slightly following the injection of Priscoline into the femoral artery, there was an early striking increase in digital volume coinciding in time with the marked flushing of the skin produced by this drug. The changes in the conjunctival vessels following Priscoline intravenously were much less marked than after C6 and were limited mainly to the venous channels. This pattern of change was interpreted as indicating that Priscoline acts primarily on the venous channels of the skin.

4. Analysis of differential alterations in the digital plethysmogram in response to acute changes such as are induced by drugs, when correlated with observations using other techniques such as direct microscopic observation of vascular reactions, may provide a method for studying the hemodynamic changes of the small vessels in man.

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